# THE ASSOCIATION BETWEEN CALCIUM ±VITAMIN D SUPPLEMENTATION AND FRACTURE RISK AMONG INCIDENT USERS OF ORAL BISPHOSPHONATES: A POPULATION-BASED COHORT STUDY

C. Reyes1 , S. Hawley2 , M. K. Javaid2 , A. Díez-Pérez3 , C. Cooper4 , D. Prieto-Alhambra2

1 GREMPAL Research Group, Institut Universitari d'Investigació en Atenció Primària Jordi Gol (IDIAP Jordi Gol), Universitat Autònoma de Barcelona, Barcelona, Spain, 2 Oxford NIHR Musculoskeletal Biomedical Research Unit, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom, 3 Musculoskeletal Research Unit and RETICEF, IMIM Research Foundation, Parc de Salut Mar and Instituto de Salud Carlos III, Barcelona, Spain, 4 MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom

**Objective:**

To analyze the association between Calcium±D supplements and fracture risk among incident users of oral bisphosphonates (BP).

**Material and Methods**:

Design: retrospective cohort study using primary/secondary care records linked to pharmacy dispensation data from the SIDIAP database (covers >5.5 million subjects from Catalonia, Spain).

Eligibility: All incident users of oral BP (2006–2007).

Exclusion criteria: Paget disease, age, <40, previous use of BP and/or supplements or <12-month BP therapy or calcium supplementation. Persistent users of ≥12 months of Calcium or Calcium+D supplements were respectively compared to supplement nonusers after matching on baseline characteristics using propensity scores (PS).

Follow-up: from 12 months after supplement initiation to the earliest of BP or supplement cessation, death, loss of followup or incident fracture (except skull/face or digits). PS were calculated using logistic regression. Fine&Gray models were fitted to study the effect of supplements on fracture, accounting for competing risk of death.

**Results**:

Study population: 297/395 Calcium only and 998/4, 061 Calcium+D users were matched to 825 and 998 nonusers, respectively. No relevant differences in baseline characteristics remained between matched subjects. Rates of fracture while on treatment were similar between matched groups; incidence rates per 100 PYs: 3.6 (95 %CI 2.2–6.0) and 2.8 (95 %CI 2.1–3.8) for calcium users and matched nonusers and 3.7 (95 %CI 2.5–5.5) and 2.8 (95 %CI 2.1–3.7) for Calcium+ D users and matched nonusers, respectively. No association was found between supplement use and fracture risk; adjusted SHR 1.27 (95 %CI 0.70–2.30) and 1.15 (95 %CI 0.69–1.91) for Calcium and Calcium+D use respectively.

**Conclusion**:

Calcium±D supplement use does not influence fracture risk among incident users of BP. Further randomized trials are needed to inform Calcium±D prescription for these patients.

**Conflict of interest**:

DPA: Unrestricted research grants from Amgen and Bioiberica; ADP: speaker or advisor for Lilly, Amgen, Pfizer, Active Life Sci; MKJ: unrestricted research grants/ speaker/ advisor for Lilly, Amgen, Internis, Consilient; C.C: personal fees from consultancy, lecture fees and honoraria from Amgen, GSK, Alliance for Better Bone Health, MSD, Eli Lilly, Pfizer, Novartis, Servier, Medtronic and Roche outside the submitted work